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Characteristics of acoustic wave propagation in dermis for the diagnosis of the superficial tissue damage in radiation therapy

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ABSTRACT

Measurement of tissue radiation damage quantitatively in radiation therapy is very important to optimize the therapeutic treatment. Ionized radiation induces homogenization of the extracellular matrix which is synthesized by fibroblast and the randomization of the orientation of the collagen fibers in dermis. If the dermis is exposed by ionized radiation, a thermal acoustic shear wave which propagates in dermis becomes harmonic wave; Otherwise, an inharmonic wave is expected because of inhomogeneous and the anisotropic properties of dermis. A polarized optical heterodyne interferometer was setup in order to measure the transverse displacement of the shear wave in order to analyze the propagation mode of the shear wave in dermis. The detection sensitivity of the displacement was 1nm and the dynamic range was 300 nm in this arrangement. The lowest dose that can be detected by the exposure of 4 MeV radiation on porcine dermis was 1 cGy.

Keywords : Dermis, interferometer, heterodyne, collagen, fibroblast, shear wave, displacement

1. INTRODUCTION

In the area of dermatology, different techniques to measure the change of linear and circular birefringence caused by the thermal damages are studied extensively[1,2]. However, the most attractive technique recently developed was the polarization sensitive optical coherence tomography(OCT). It can be used to sense birefringence image caused by the thermal damages tomographically[3,4]. The thermal denaturation of collagen which is from α-helix to a random-coil conformation that is accompanied by a loss of birefringence[2]. In loose connective tissue like dermis is highly cellular and contains numerous fibroblasts which synthesize much of the extra-cellular matrix and collagen fibers. However, at least 40℃ of temperature is required to result thermal denatureation of dermis[2,4]. In contrast, the ionized radiation induces the denaturation of collagen fibers and the extra-cellular matrix in dermis is examined in this paper[5-7]. According to the percentage depth dose of 4 *MeV* photon radiation, the radiation dose is built up in dermis[7] which contains abundant collagen fibers and fibroblasts[5]. The orientation of collagen fibers is then randomized their orientation by the exposure of radiation. Meanwhile, the extra-cellular matrix is enforced lost the structure and becomes homogeneous[5,6] as well. For a living tissue, if the dose of the exposure does not induced a permanent damage, the dermis is able to repair itself the and recovers the dermis back to inhomogeneous

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and anisotropic as it was before the exposure. A thermal acoustic wave which propagates in dermis then becomes inharmonic from the harmonic sinusoidal wave which propagates in a isotropic and homogeneous medium. In a bulk isotropic material, there are thermal acoustic shear wave and longitudinal wave propagating in the medium[8]. However, the shear wave displaces in X direction is in the direction perpendicular to the propagation in Z-axis while the longitudinal wave displaced in Z direction is in the direction parallel to Z-axis. Because dermis is so sensitive to the ionization radiation that induces dermis homogeneously and isotropically. Therefore, a harmonic thermal acoustic shear wave is expected propagation in dermis at room temperature. A polarized optical heterodyne interferometer which measures the transverse displacement of the shear wave is setup in order to analyzer the harmonic mode of the shear wave. Then, a highly sensitive biological ionization radiation sensor is demostrated.

2. PRINCIPLE

There are a thermal acoustic longitudinal wave and a two shear waves propagating in the bulk of isotropic and homogeneous material when the material reaches the thermodynamic equilibrium with its surroundings[8]. The speed of propagation of the longitudinal wave is faster than shear wave[8]. The equation of the thermal acoustic longitudinal wave can be expressed

$$\frac{\partial \bar{\mu}_\ell}{\partial t^2} - v_\ell^2 \nabla^2 \bar{\mu}_\ell = 0 \tag{1}$$

and the thermal acoustic shear wave is

$$\frac{\partial \bar{\mu}_s}{\partial t^2} - v_s^2 \nabla^2 \bar{\mu}_s = 0 \tag{2}$$

where v_ℓ and v_s are the propagation speed of the longitudinal wave and the shear wave respectively. $\bar{\mu}_\ell$ and $\bar{\mu}_s$ are the displacements with respect to the longitudinal wave and the shear wave. It is because the exposure of the ionized radiation induces extra-cellular matrix and the collagen fibers in dermis homogeneously and isotropically. Therefore, a polarized optical heterodyne interferometer is setup in order to analyze the propagation mode of the thermal acoustic shear wave in dermis[9]. A beam splitter (BS1) divides the laser beam into a reference beam and a signal beam. According to theory, a linear polarized light can be separated into two orthogonal linear polarized waves, P wave and S wave, which propagate in the Mach-Zehnder interferometer simultaneously. There are two acoustic-optic modulators---AOM1 and AOM2---in the interferometer where P wave and the S wave are simultaneously modulated. A polarized beam splitter (PBS1) divides the signal beam into P_1 wave and S_1 wave which are driven by AOM1 at frequency ω_s. P_1 wave is incident onto the test sample T. While the S_1 wave is onto the reference mirror R. Both P_1 wave and S_1 wave are reflected back to the interferometer. Similarly, P_2 wave and S_2 wave which are driven by AOM2 at frequency ω_r propagate in the reference beam. The P_1 and P_2 waves are separated from S_1 and S_2 waves by PBS2 and are detected and heterodyned at D_p and D_s respectively. The intensities of the heterodyned P wave (P_1+P_2) and S wave (S_1+S_2) are

$$\mathbf{I}_p(\Delta\omega t) = \left| \mathbf{A}_{p_1} \exp[\, i(\omega_s t + \phi_{p_1})] + \mathbf{A}_{p_2} \exp\, i[\omega_r t + \phi_{p_2}] \right|^2$$

$$= \mathbf{I}_{p_1} + \mathbf{I}_{p_2} + 2(\mathbf{I}_{p_1}\mathbf{I}_{p_2})^{1/2} \cdot \cos(\Delta\omega t + \Delta\phi_p) \tag{3}$$

$$I_s(\Delta\omega t) = \left| A_{s_1} \exp(i(\omega_s t + \phi_{s_1})) + A_{s_2} \exp(i(\omega_r t + \phi_{s_2})) \right|^2$$

$$= I_{s_1} + I_{s_2} + 2(I_{s_1} I_{s_2})^{1/2} \cdot \cos(\Delta\omega t + \Delta\phi_s) \quad (4)$$

where $\Delta\omega = \omega_s - \omega_r$ is the beat frequency of the signal beam and the reference beam. $\Delta\phi_p = \phi_{p_1} - \phi_{p_2}$ and $\Delta\phi_s = \phi_{s_1} - \phi_{s_2}$ are the phases difference of the heterodyne P wave and S wave respectively. A lock-in amplifier is chosen to measure the phase difference $\Delta\phi = \Delta\phi_p - \Delta\phi_s = \phi_{p_1} - \phi_{s_1}$ and the amplitude at the same time. Besides, the measurement of the amplitude ratio of the heterodyne P wave and S waves, which is $(\frac{I_{p_1} I_{p_2}}{I_{s_1} I_{s_2}})^{1/2}$ enables us to monitor the degradation of the heterodyned efficiency in real time. A phase difference $\Delta\phi$ between the heterodyned P wave and S wave relates to the relative displacement Δh between the test surface T and the reference mirror R. The relation is $\Delta\phi = \frac{4\pi}{\lambda}\Delta h$. λ is the wavelength of the laser source. When a thermal acoustic shear wave is propagating in dermis at room temperature. A transverse displacement of the shear wave can be monitored in real time by the interferometer. Then a propagation mode of the thermal acoustic shear wave is analyzed following the variation of the transverse displacement versus time. Therefore a highly sensitive biological ionized radiation sensor in terms of the propagation mode analysis of the thermal shear wave is introduced.

3.Experimental Setup

A shown in Fig.1, a linearly polarized frequency stabilized He-Ne laser (Spectra Physics, Model 117A) in conjunction with a $\frac{\lambda}{2}$ wave plate and an optical isolator were used in the configuration. A laser beam which was divided into two equal amplitude by a beam splitter (BS1) was incident on the Mach-Zehnder interferometer. Two modulators--AOM1 and AOM2--were driven at frequencies of ω_r=80.0000 MHz and ω_s=80.0377 MHz, respectively. A beat frequency of 33.7-kHz of the heterodyned P and S waves was generated by the detector D_p and D_s respectively. To obtain a better signal-to-noise ratio, a bandpass filter with the central frequency at 33.7 kHz was required behind each detector. The stability of the phase and the amplitude of the interferometer were ± 0.2°/hr and ± 0.3 %/hr in the experiment. It corresponded to 1 nm resolution in transverse displacement. The dynamic range of the displacement was 300 nm . A 40X objective (N.A.=0.65) was used to focus the P_1 wave onto the sample which was a 5× 8 cm porcine dermis of 0.3 mm in thickness[10]. The lateral resolution was 0.6 μm. Before radiation exposure an irregular inharmonic thermal acoustic shear wave was observed in the experiment as shown in Fig2.. A 5nm variation of the transverse displacement was measured. Figure 3(a), shows the transverse displacement of a harmonics shear acoustic wave in porcine dermis of 1cGy dose by 4MeV photon exposure using Varian 2100C LINAC. Fig.3(b) shows the displacement response of the shear wave 30 minutes later. The result confirms the repair ability of the living porcine dermis that an irregular inharmonic wave propagated in the porcine dermis. The displacement of the thermal acoustic shear wave was an order of 30 nm in the measurement. After a 10Gy radiation dose of 4MeV photon radiation exposure on the porcine dermis.Fig.4(a) presents the response of harmonic shear wave as we expected. However, a

analysis of the displacement of the shear wave 24 hrs later, Fig.4(b) shows the some response of the shear wave of the porcine dermis that was unable to repair itself biologically. Therefore, a ionized radiation sensitive biological sensor is introduced. A polarized optical heterodyne interferometer was used to sense the propagation mode of the thermal shear wave in porcine dermis is demonstrated experimentally. The lowest dose of the exposure was 1cGy that strengthens the detection sensitivity of ionized radiation in comparison with the method in radiation biology[6].

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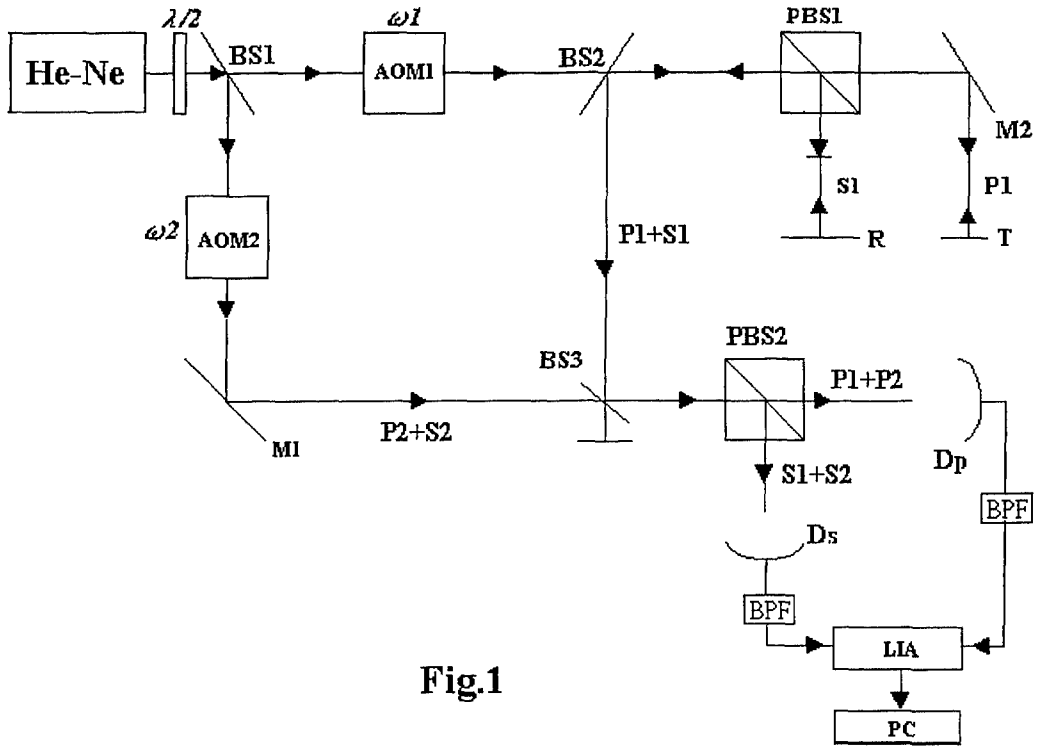
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λ/2
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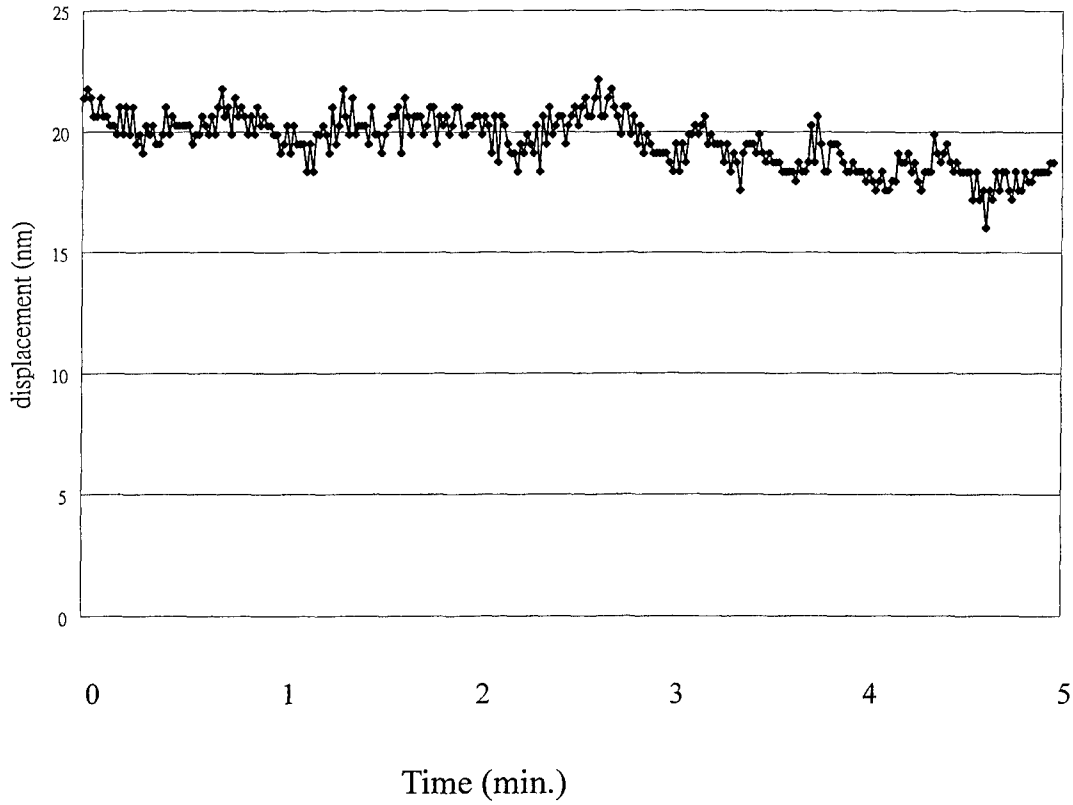
ω1
AOM1
BS2
PBS1
M2
S1
P1
R
T
ω2
AOM2
P1+S1
PBS2
BS3
P1+P2
M1
P2+S2
S1+S2
Dp
BPF
Ds
BPF
LIA
PC

Fig.1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10
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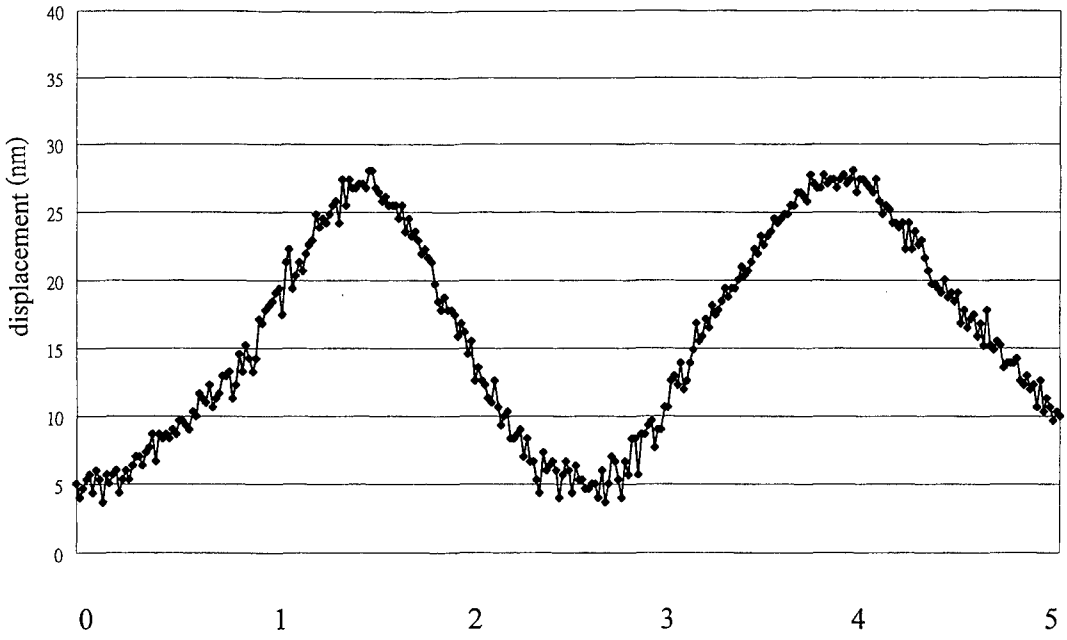
1
2
3
4
5
Time (min.)

Fig.2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35
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displacement (nm)
0
1
2
3
4
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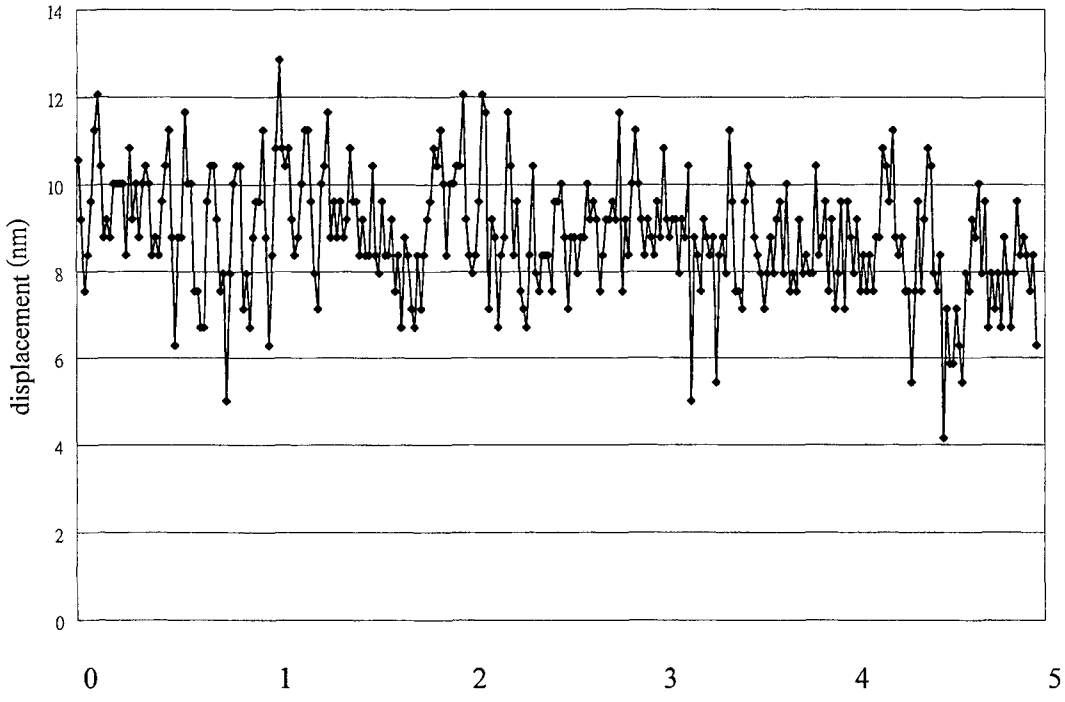
Time (min.)

Fig.3（a）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Time (min.)

Fig.3（b）

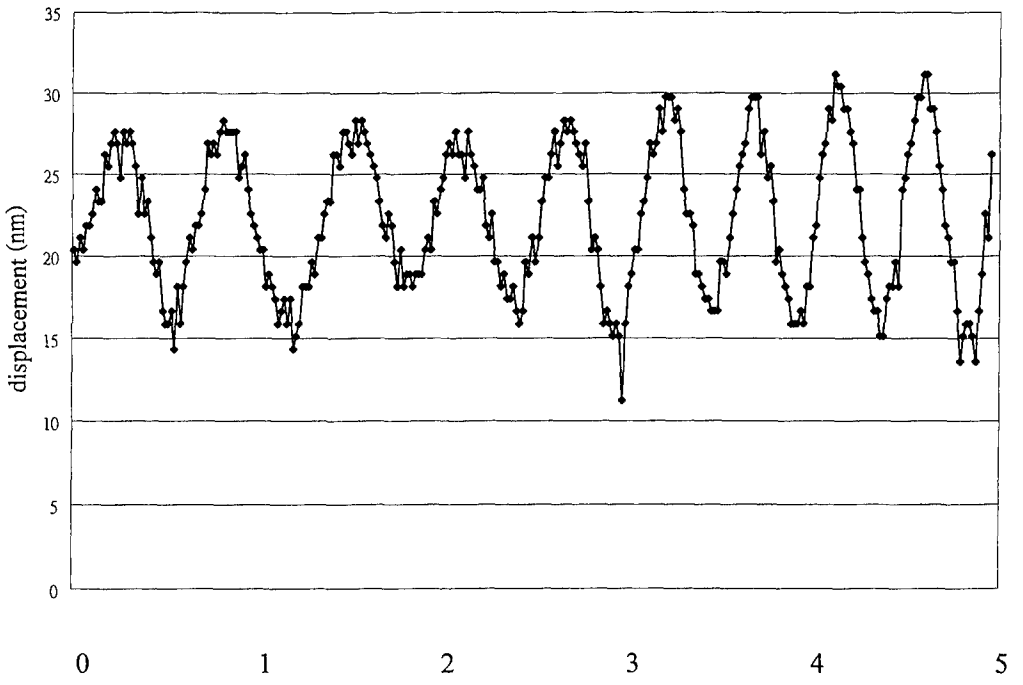
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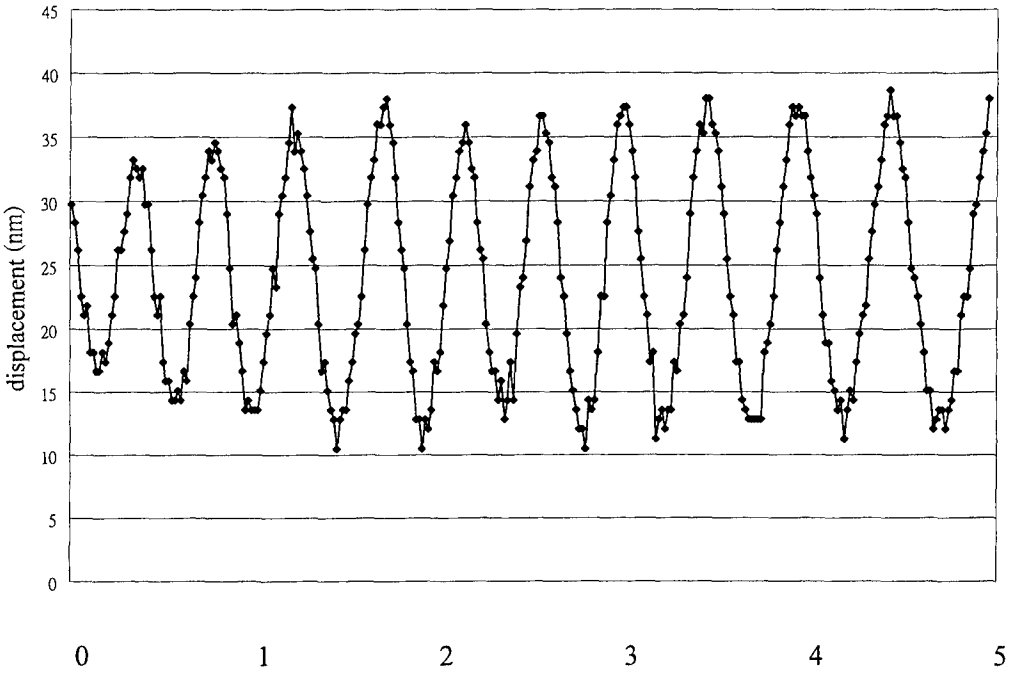
Fig.4（a）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15
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displacement (nm)
0
1
2
3
4
5
Time (min.)

Fig.4（b）